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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|-----------------------------------|------------------------|
| 10/692,724 | 10/27/2003 | Joseph Loscalzo | 102258.170 US3 | 9697 |
| 25270 7590 09/20/2007 WILMERHALE/NITROMED 1875 PENNSYLVANIA AVE, NW WASHINGTON, DC 20006 | | | EXAMINER SRIVASTAVA, KAILASH C | |
| | | | ART.UNIT 1657 | PAPER NUMBER |
| | | | MAIL DATE 09/20/2007 | DELIVERY MODE PAPER |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|---------------------------------------|---------------------------------|--|
| Office Action Summary | Application No. 10/692,724 | Applicant(s) LOSCALZO ET AL. | |
| | Examiner Dr. Kailash C. Srivastava | Art Unit 1657 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 June 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3, 6-10, 21 and 22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 6-10, 21 and 22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Response and amendment filed 20 June 2007 in response to Office Action mailed 11 April 2007 is acknowledged and entered.
2. In view of applicants' remarks filed 20 June 2007, following rejections in the Office Action mailed 11 April 2007 are hereby withdrawn:
 - a. Indefiniteness rejection to Claims 1 and 21-22 under 35 U.S.C. §112, 2nd paragraph;
 - b. Rejection to Claims 1-10 and 21-22 under 35 U.S.C. §102(b) as anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over Del Soldato (WO 99/00361);
 - c. Rejection to Claims 1-10 and 21-22 under 35 U.S.C. §103 (a) as obvious over combined teachings from Del Soldato (WO 99/00361) in view of Chobanian et al (U. S. Patent 5,645,839).

CLAIMS STATUS

3. Claims 4-5, 11-20 and 23-37 have been cancelled.
4. Claims 1, 3 and 6 have been amended.
5. Claims 1-3, 6-10 and 21-22 are pending and are examined on merits.

Claim Rejections - 35 U.S.C. §112

First Paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-3, 6-10 and 21-22 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement.
8. Claims 1-3, 6-10 and 21-22 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In response to rejections made in the Office action mailed 11 April 2007 under 35 U.S.C. §112,

first paragraph to Claims 1-3, 6-10 and 21-22, applicants argue that “one of skill in the art would understand how to prepare nitrosated ACE inhibitors from any and all of the parent ACE inhibitors listed at Page 30 of specification. Applicants also argue that the WO 99/00361 reference recited in the specification discloses ACE inhibitor nitrate salts which are not the same as nitrosated ACE inhibitors (See, Remarks filed 20 June 2007 at Page 5, Lines 13-26). Applicants further argue that they also have demonstrated in the specification the following (See Remarks filed 20 June 2007, Page 5, Line 28 to Page 6, Line 8):

- a method to treat “a cardiovascular disease through administration of a ntrosated ACE inhibitor or a salt thereof” ;
- adequate guidance to make solid dosage forms of the nitrosated ACE inhibitors;
- methods of administering the dosage forms to a patient in need thereof;
- one skilled in the art would be able to determine the appropriate dose using standard clinical techniques as described in The Physician’s Desk Reference (See Specification, Page 36, Line 25);
- one skilled in the art would be able to determine and adjust the dose accordingly, depending upon patient profile (Specification pages 36-37).

Applicants are correct is arguing that the specification teaches:

- How to prepare nitrosated ACE inhibitors;
- The WO 99/00361 reference teaches ACE inhibitor nitrate salts and preparation thereof and those are not the same as nitrosated ACE inhibitors;
- a method to treat “a cardiovascular disease through administration of a ntrosated ACE inhibitor or a salt thereof” ;
- adequate guidance to make solid dosage forms of the nitrosated ACE inhibitors, wherein said dosage forms are tablets or a pharmaceutical carrier; and
- methods to administer the dosage forms to a patient in need thereof.

The written description requirement and enablement rejections cited *supra*, are, however, based on the lack of recitation in the description of determining the therapeutic dosage and adjustment of therapeutic dosage for a patient in need of a nitrosated ACE inhibitor since the “Physician’s Desk Reference” and recitation in the specification guides the dosage for nitrate salts of ACE inhibitors (e.g., isosorbide mono or dinitrate), not the nitrosated ACE inhibitors (See Specification, Page 37, Lne 29 to

Page 38, Line 17). As applicants argue, the ACE inhibitor nitrate salts are not the same as nitrosated ACE inhibitors (See, Remarks filed 20 June 2007, Page 5, Lines 25-26). Consequently, the specification as presented currently lacks written description for a “therapeutically effective amount” of a “nitrosated ACE inhibitor” as claimed in Claim 1 and the claims dependent on Claim 1. Therefore, the specification lacks enablement for the claimed invention and is not affirmative that the applicants indeed have the possession of the claimed invention as claimed currently.

Applicants’ arguments filed 20 June 2007 regarding the rejection to Claims 1-3, 6-10 and 21-22 under 35 U.S.C. § 112, 1st paragraph in the Office Action mailed 11 April 2007 have been fully and carefully considered, but are not persuasive for the reasons:

- (i) discussed *supra*; and
- (ii) of record at pages 5-9, items 11-14 in the Office Action mailed 11 April 2007.

Therefore, the rejection to Claims 1-3, 6-10 and 21-22 under 35 U.S.C. § 112, 1st paragraph in the Office Action mailed 11 April 2007 is maintained and is adhered to.

CONCLUSION

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).


A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. For the aforementioned reasons, no claims are allowed.


11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached at (571)-272-0925 Monday through Thursday 7:30 A.M. to 6:00 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.


Kallash C. Srivastava, Ph.D.
Patent Examiner
Art Unit 1657
(571) 272-0923

11 September 2007


DAVID M. NAFF
PRIMARY EXAMINER
ART UNIT 128/657